

300.4, 311, 301, 13, 295.70), schizophrenia and related disorders (295, 297.1, 298.9, 297.3, 298.9), anxiety disorders (300.XX, 309.81, 308.3), adjustment disorders (309, XX) and personality disorders (codes 301. XX).

✓ 8. (Amended) A method of identifying at least one human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder which comprises fragmentation of a YAC clone as defined in claim 2 [any one of claims 2 to 4] and detection of nucleotide triplet repeats.

✓ 9. (Amended) A method as claimed in claim 7 [or 8] wherein said repeated triplet is CAG or CTG.

✓ 11. (Amended) A method of identifying at least one human gene including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder wherein said gene is present in the DNA comprised in the YAC clones as defined in claim 2 [any one of claims 2 to 5], which method comprises the step of detecting an expression product of said gene with an antibody capable of recognising a protein with an amino acid sequence comprising a string of at least 8 continuous glutamine residues.

13. (Amended) A method as claimed in claim 11 [or claim 12] wherein said antibody is mAB 1C2.

✓ 14. (Amended) A method of preparing a contig map of YAC clones of the region of human chromosome 18q between polymorphic markers D18S60 and D18S61 which comprises the steps of:

(a) subcloning the YAC clones according to claim 2 [any one of claims 2 to 5] into exon trap vectors;

(b) using the nucleotide sequences shown in any one of Figures 1 to 11 or any other known sequence tagged sequence from the YAC contig described herein, or part thereof consisting of not less than 14 contiguous bases or the complement thereof, to detect overlaps among the cosmid vectors, and

(c) constructing a cosmid contig map of a YAC clone of said region.

✓ 16. (Amended) A method of identifying at least one human gene or mutated or polymorphic variants thereof which is associated with a mood disorder or related disorder which comprises the steps of:

(a) subcloning the YAC clones according to claim 2 [any one of claims 2 to 5] into a cosmid, BAC, PAC or other vector;

(b) using the nucleotide sequences shown in any one of Figures 1 to 11 or any other known sequence tagged sequence from the YAC contig described herein, or part thereof consisting of not less than 14 contiguous bases or the complement thereof, to detect overlaps amongst the subclones and construct a map thereof;

(c) identifying the position of genes within the subcloned DNA by one or more of CpG island identification, zoo-blotting, hybridization of said subcloned DNA to a cDNA library or a Northern blot of mRNA from a panel of culture cell lines;

(d) detecting differences between said genes and equivalent regions of the DNA of an individual afflicted with a mood disorder or related disorder; and

(e) identifying said gene which, if defective, is associated with said mood disorder or related disorder.

✓ 17. (Amended) An isolated human gene, including mutated or polymorphic variants thereof, which is associated with a mood disorder or related disorder which is obtainable by the method according to claim 7 [any of claims 7 to 13, 15 or 16].

✓ 19. (Amended) A cDNA encoding the protein of claim 18 which is obtainable by the method of claim 7 [any one of claims 7 to 13, 15 or 16].

✓ 28. (Amended) A method as in claim 26 [or 27] which comprises the steps of:

- obtaining a DNA sample from said individual;
- providing primers suitable for the amplification of a nucleotide sequence comprised in the sequence shown in any one of Figures 15a, 16a, 17a or 18a said primers flanking the trinucleotide repeats comprised in said sequence;
- applying said primers to the said DNA sample and carrying out an amplification reaction;
- carrying out the same amplification reaction on a DNA sample from a control individual; and
- comparing the results of the amplification reaction for the said individual and for the said control individual;

wherein the presence of an amplified fragment from said individual which is bigger in size from said individual which is bigger in size from that of said control individual is an

indication of the presence of a susceptibility to a mood disorder or related disorder of said individual.

✓ 40. (Amended) An expression vector which comprises a sequence of nucleotides as claimed in claim 21 [claims 21 or 22].

✓ 41. (Amended) A reporter plasmid which comprises the promoter region of a nucleic acid molecule as claimed in claim 21 [or 22] positioned upstream of a reporter gene which encodes a reporter molecule so that expression of said reporter gene is controlled by said promoter region.

✓ 43. (Amended) An eukaryotic cell or multicellular tissue or organism comprising a transgene encoding a protein as claimed in claim 23 [claims 23 or 24].

✓ 44. (Amended) A method for determining if a compound is an enhancer or inhibitor of expression of a gene associated with a mood disorder or related disorder which comprises the steps of:

- a) contacting a cell as claimed in claim 42 with said compound;
- b) detecting and/or quantitatively evaluating the presence of any mRNA transcript corresponding to a nucleic acid as claimed in claim 21 [or 22]; and
- c) comparing the level of transcription of said nucleic acid with the level of transcription of the same nucleic acid in a cell as claimed in claim 42 not exposed to said compound[;].

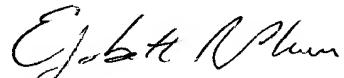
✓ 45. (Amended) A method for determining if a compound is an enhancer or inhibitor of expression of a gene associated with a mood disorder or related disorder which comprises the steps of:

- a) contacting a cell as claimed in claim 42 with said compound;
- b) detecting and/or quantitatively evaluating the expression of a protein as claimed in claim 23 [claims 23 or 24]; and
- c) comparing the level of expression of said protein with that of the same protein in a cell not exposed to said compound.

✓ 47. (Amended) A compound identified as an enhancer or an inhibitor of the expression of a gene associated with a mood disorder or related disorder by a method as claimed in claim 44 [claims 44 to 46].

If any other information is needed, please contact the undersigned attorney by phone (617-720-3500, Ext. 343) to expedite the further prosecution of this patent application.

Respectfully submitted,



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